

DETAILED ACTION

1. Claims 1-11, 13-14 are pending.

Priority

2. This application is a 371 of PCT/EP05/50708 filed 02/17/2005, which claims priority to EUROPEAN PATENT OFFICE (EPO) 04003592.5 filed 02/18/2004.

Response to Restriction Election

3. Applicant's election of Group II and the species (Example 4) in the reply filed on January 14, 2008 (clarified in the interview summary attached) is acknowledged. The election was made with traverse, and the examiner finds the arguments unpersuasive. The traversal is on the grounds that the restriction requirement failed to explain the reasons for a serious burden for searching the invention. Search burden is actually not a criterion for restriction of applications filed under 35 U.S.C. 371, but rather the presence of a special technical feature which was shown to be lacking from the instant claims is the standard in such applications. The unity of invention standard applies in applications filed under the Patent Cooperation Treaty (PCT) and is mentioned in Rule 13.1 (See MPEP Chapter 1800). However out courtesy to the applicant and in order to advance prosecution the examiner has rejoined groups I-III to make a new group I (encompassing the previous groups I-III). The previous group IV is now group II and the previous group V is now group III. The revised requirement is shown below:

Revised restriction requirement:

Group I, Claims 1-11 drawn to compounds and compositions reading on claim 1, R7 is (b) or (c) where R11 and R10 or R14 and R15 form piperazine drawn to piperazines; compounds and compositions reading on claim 1, R7 is (b) or (c) where R11 and R10 or R14 and R15 form azocan-1-yl drawn to azocanes, and compounds and compositions reading on claim 1, R7 is (a) (b) or (c) where R11 and R10 or R14 and R15 are limited to H, alkyl, or cycloalkyl drawn to phenanthridines.

Group II, Claims 1-11 drawn to all other compounds and compositions not encompassed by Groups I-III, reading on for example claim 1, R7 is (d) drawn to purines. If this group is elected, a further election of a single disclosed species is also required. Further restriction based on the election will be made.

Group III, Claim 13-14, drawn to methods of treating “illnesses”, limited in scope to one of the compounds of groups I-IV. If this group is elected, a single disclosed species of compound useful in treating “illnesses” and the election of a single disclosed “illness”, is also required. Further restriction based on the election will be made.

This application contains claims drawn to a nonelected invention with traverse. A complete reply to this action must include a cancellation of nonelected claims or other appropriate action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

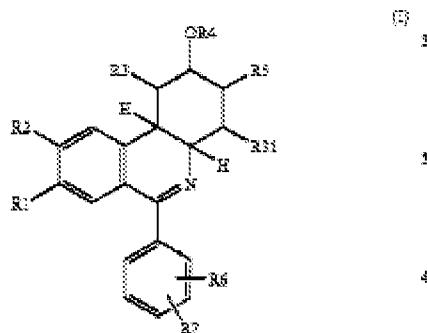
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claims 1-11 are provisionally rejected under 35 U.S.C. 103(a) as being obvious over U.S. 7,329,676 in view of US Pre-Grant Publication US 2006/0116518. The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the references, they constitute prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention “by another”; (2) a showing of a date of invention for the claimed subject

matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2). The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

- A) Determining the scope and contents of the prior art.
- B) Ascertaining the differences between the prior art and the claims at issue.
- C) Resolving the level of ordinary skill in the pertinent art.
- D) Considering objective evidence present in the application indicating obviousness or nonobviousness.

A) Determining the scope and contents of the prior art: U.S. 7,329,676 teaches a genus of compounds shown below, in particular the ‘676 definitions of R4 where both H, and alkylcarbonyl are listed as part of the genus:



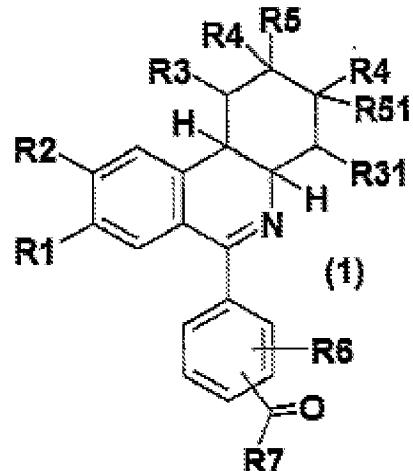
in which

R1 is hydroxyl, 1-4C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkyloxymethyl, or completely or predominantly fluorine-substituted 1-4C-alkoxy,
R2 is hydroxyl, 1-4C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkyloxymethyl, or completely or predominantly fluorine-substituted 1-4C-alkoxy,

or in which

R1 and R2 together are a 1-2C-alkylcarboxy group,
R3 is hydrogen or 1-4C-alkyl,
R31 is hydrogen or 1-4C-alkyl,
R4 is hydrogen, 1-4C-alkyl, completely or predominantly fluorine-substituted 1-4C-alkyl, 1-4C-alkoxy-1-4C-alkyl, hydroxy-1-4C-alkyl or 1-7C-alkylcarbonyl,
R5 is hydrogen or 1-4C-alkyl,
R6 is hydrogen, 1-4C-alkyl, trifluoromethyl, 1-4C-alkoxy, completely or predominantly fluorine-substituted 1-4C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkyloxymethyl, halogen, nitro, cyano, hydroxyl, 1-4C-alkylcarbonyloxy, amino, mono- or di-1-4C-alkylamino, phenyl, phenyl-1-4C-alkyl, 1-4C-alkylcarbonylamino, phenoxy or C(O)OR1, wherein

US Pre-Grant Publication US 2006/0116518 teaches a genus of compounds bearing the guanidinyl moieties at R7, but differ in the identity of the R4 or R5 group. A relevant portion is shown below:



in which

R1 is hydroxyl, 1-4C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy or completely or predominantly fluorine-substituted 1-4C-alkoxy, and

R2 is hydroxyl, 1-4C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy or completely or predominantly fluorine-substituted 1-4C-alkoxy,

R1 and R2 together are a 1-2C-alkylenedioxy group,

R3 is hydrogen or 1-4C-alkyl,

R31 is hydrogen or 1-4C-alkyl,

or in which

R3 and R31 together are a 1-4C-alkylene group,

R4 is hydrogen or 1-4C-alkyl,

R5 is hydrogen,

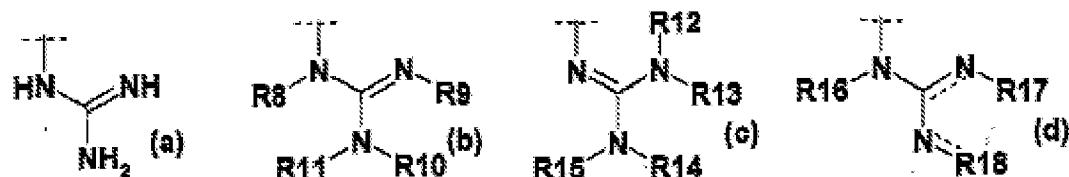
R51 is hydrogen,

or in which

R6 and R51 together represent an additional bond,

R6 is hydrogen, halogen, nitro, 1-4C-alkyl, trifluoromethyl or 1-4C-alkoxy,

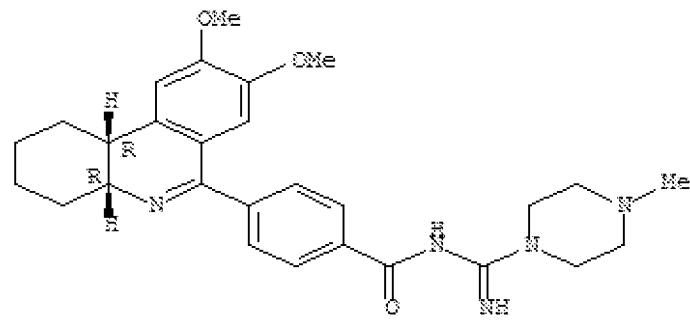
R7 is a radical of formulas (a), (b), (c) or (d)



A specific compound which bears the piperazinyl moiety of the instantly elected species is shown below:

RN 667422-58-5 CASLUS
CN Benzamide, 4-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-N-[imino(4-methyl-1-piperazinyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



B) Ascertaining the differences between the prior art and the claims at issue.

The instant claims are drawn to compounds that differ from the US Pre-Grant Publication US 2006/0116518 by the definition of R4, and U.S. 7,329,676 teaches very similar compounds that have this alkoxy carbonyl or hydroxy modification. In the alternative, the instantly claimed compounds may be seen as variants of the '676 application which have the R⁷ modification as taught by US Pre-Grant Publication US 2006/0116518.

C) Resolving the level of ordinary skill in the pertinent art: The level of ordinary skill is high. Someone preparing these compounds would be trained in organic chemistry and would recognize the very close structural similarity and would expect them to have similar properties.

D) Considering objective evidence present in the application indicating obviousness or nonobviousness: The compounds of the claims at hand are analogs of old compounds. One of ordinary skill would be motivated to make the compounds of the invention because he would

expect the compounds to have similar properties, indeed we see that these compounds are both potent inhibitors of PDE4. *In re Grabiak* 226 USPQ 870, "[w]hen chemical compounds have "very close" structural similarities and similar utilities, without more a *prima facie* case may be made", *In re Deuel* 34 USPQ2d 1210, "a known compound may suggest its **analog**s or isomers, either geometric isomers (*cis* v. *trans*) or position isomers (emphasis added) (e.g. *ortho* v. *para*)".

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 1-11 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. patent 7,329,676 in view of US Pre-Grant Publication US 2006/0116518. A detailed discussion of this rejection can be found in the 103(a) rejection above which is founded in the same reasoning and documents.

6. Claims 1-11 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims of copending Application No. 10/524,634 in view of US Patent 7,329,676 . A detailed discussion of this rejection can be found in the 103(a) rejection above which is founded in the same reasoning and documents.

This is a provisional obviousness-type double patenting rejection.

7. The examiner has also identified fifteen applications with the inventor in common, all with similar titles and subject matter: 10/524820, 10/589082, 10/590803, 10/590805, 10/591472, 10/591478, 10/591480, 10/591768, 11/661369, 11/661377, 11/795981, 11/884934, 11/884935, 11/885425, 12/000710. The burden is now shifted to the applicant to provide information regarding any instance of double patenting in view of the rejections above.

Conclusion

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David K. O'Dell whose telephone number is (571)272-9071. The examiner can normally be reached on Mon-Fri 7:30 A.M.-5:00 P.M EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Primary examiner, Rita Desai can be reached on (571)272-0684. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the

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Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

D.K.O.

/Rita J. Desai/
Primary Examiner, Art Unit 1625